REMARKS

The Pending Claims

Claims 1-25 are currently pending. No claim is currently allowed.

1. Rejection under 35 U.S.C. § 103

Claims 1-25 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Laugharn *et al* (U.S. Patent No. 6,120,985; hereinafter "Laugharn") in view of Smith *et al*. (U.S. Patent No. 6,310,199; hereinafter "Smith"). (Office Action, page 3.) Applicant respectfully disagrees but in order to advance prosecution has amended claim 1.

Applicant has amended claim 1 to recite "a plurality of particulate solid supports." Support for the term "particulate" can be found *inter alia* at page 37, lines 11-19 of the specification. Applicant has further amended claim 1 to recite "protein components contained in said sample become bound to the solid supports by effecting a chromatographic interaction." Support for binding by a chromatographic interaction may be found, *inter alia*, in Example 4 of the specification. These amendments do not add new matter. Applicant respectfully submits that none of the cited combinations of references render the claimed invention *prima facie* obvious. The obviousness analysis under 35 U.S.C. § 103(a) requires the consideration of the scope and the content of the prior art, the level of skill in the relevant art, and the differences between the prior art and the claimed subject matter. *Graham v. John Deere Co.,* 383 U.S. 1, 17 (1966). Applicants note that if a modification changes the principle of operation of a reference, then there cannot be said that a reasonable expectation of success exists.

Laurghan describes a method and apparatus for isolating nucleic acids from a sample. The method combines cell lysis by maintaining the cells at sub-zero temperature and exposing them to elevated pressure, in a repeated cycle. The isolation of nucleic acid is achieved by applying an initial pressure which allows sequence independent binding of the nucleic acid to the solid phase. The pressure is then modified to disrupt binding of the nucleic acid to the solid phase, and release the nucleic acids which are then transported away from the solid phase, for example using electrophoresis or electroosmosis. In view of the fact that lysis and nucleic acid isolation is carried out in the same device, it is necessarily complex. It comprises a tubular structure housing a cartridge, which in turn houses the solid phase to which the nucleic acid

becomes bound. The sample (i.e. the lysed cells) from which the nucleic acid is isolated flows into a first opening in the cartridge, past the solid phase where nucleic acid is removed, and out through a second opening in the cartridge (column 19, lines 5 to 18).

Laurghan is almost entirely directed towards isolating nucleic acids from a lysed cellular sample, and refers only in passing to the possibility of extracting other biological materials from the sample, such as proteins and lipids. As noted by the Examiner, in the paragraph bridging columns 19 and 20, the cartridges may contain multiple, layered resins for example a cation-exchange resin to capture positively charged proteins and a hydrophobic (e.g. reverse-phase) resin to bind lipids in the sample.

The use of magnetic particles as a solid phase is not contemplated by Laurghan. In fact, a lengthy list of possible solid phases is provided in the paragraph bridging columns 1 and 2 of Laurghan, but notably excludes magnetic particles. The Examiner has cited Smith as teaching the use of magnetic particles, which he believes when combined with Laurghan would lead to the present invention.

Smith disclose the use of ion exchange chromatography matrices, including magnetic beads, in isolating nucleic acids away from contaminants such as proteins, lipids and sugars from a sample. The method described relies on pH dependent binding and release of the biological material from the solid phase.

Contrary to the Examiner's assumption, a person skilled in the art at the priority date of the invention would not have been motivated to apply the teaching of Smith to Laurghan, and replace the solid phase with magnetic particles. In Laurghan, the solid phase is immobile, and the nucleic acid is extracted from a sample as it flows past. Despite detailed discussion of the apparatus and method by Laurghan, they do not suggest using magnetic particles, or indeed, a mobile solid phase. In fact, a key feature of the device throughout the teaching of Laurghan is that the solid phase is static.

Indeed, there would have been no advantage in replacing the static solid phase of Laugharn with a mobile solid phase such as magnetic particles, since there is no required movement or handling of the solid phase resin with biological material bound thereto, in Laurghan. If magnetic beads were used in Laurghan, a complete redesign of the device would be required, to move from a closed system of the cartridge, to an open system where the beads could be accessed for transfer to downstream analysis.

Further, it would not even be appropriate to use magnetic particles in the Laurghan technology, because in order to release the nucleic acid molecules from the resin by a change in pressure, the resin must be in a liquid environment, therefore requiring dilution of the bound molecules prior to downstream analysis. This would be contrary to one of the reasons for using magnetic particles, which is that "dry" particles having biological material bound thereto can be introduced into many downstream processes without eluting off the material.

It could also be said that had there been any advantage in using magnetic particles in the device of Laurghan, and if this was obvious as suggested by the Examiner, then Laurghan would have included this embodiment in their application, magnetic particles being known at that time.

Amended claim 1 recites, in part, "protein components contained in said sample become bound to the solid supports by effecting a chromatographic interaction." At page 17, lines 18-29 of the specification chromatographic interactions are described as "a solid phase which has surface chemistry which effects classical chromatography interactions such as ion exchange (including both anion exchange and cation exchange), reverse phase interactions or hydrophobic interactions."

In contrast however, Laugharn discloses in the first paragraph of the Summary of the Invention (column 1 line 50-53) "[t]he invention is based on the discovery that hydrobaric, hydrostatic pressure reversibly alters the partitioning of biomolecules between certain adsorbed and solvated phases relative to partitioning at ambient pressure". Thus, the presently claimed invention is directed in part to methods relating to ion exchange, reverse phase or hydrophobic interactions while the cited art is directed to hydrobaric/hydrostatic pressure and the partitioning of biomolecules. Given the differing modes of operation between the presently claimed invention and the cited art, one skilled in the art would not have a reasonable expectation of success in applying the teachings of Laugharn.

The presently claimed invention is to isolate and analyze the nucleic acid, RNA and protein, from a sample, which allows expression analysis in a simple manner. Laurghan are predominantly focused toward isolation of nucleic acid, and there is not sufficient motivation provided therein to lead the skilled person to develop a new method, using a solid phase completely different to that of Laurghan, for doing so. Smith are also concerned only with nucleic acid isolation, and do not provide the necessary motivation.

Even if Smith, which use magnetic beads, were used as the starting point, the skilled person would not be led to the present invention. Working in the field of Smith, there would simply be no motivation to consider the disclosure of Laurghan, which relating to "pressure-enhanced extraction and purification" would not have been considered sufficiently close in technology to warrant reviewing. Thus, the skilled person would not have even been led to the idea of multiple surfaces for binding multiple types of biological material, and certainly would not have envisaged the present invention.

In view of the above, none of the cited references, alone or in combination, teach or suggest the binding of target proteins to solid supports having a surface capable of effecting a chromatographic interaction wherein the solid supports to which nucleic acids components are bound are distinct from the solid supports to which protein components are bound, and wherein the solid support are in the form of magnetic particles as recited in independent claim 1.

Accordingly, Applicant request reconsideration and withdrawal of the rejection of claims 1 - 25 under 35 U.S.C. § 103.

CONCLUSION

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.
Prompt and favorable consideration of this Reply is respectfully requested.

Respectfully submitted,

/Peter G. Foiles/

Peter G. Foiles, Ph.D.
Reg. No. 46,477
(240) 379-4173.

February 22, 2010